May 23, 1994

COMMENTS ON
MADISON COUNTY LEAD EXPOSURE STUDY, GRANITE CITY, ILLINOIS

Allan H. Marcus
Environmental Criteria and Assessment Office
Environmental Protection Agency
Research Triangle Park, NC 27711

Karen Hogan
Office of Pollution Prevention and Toxics
Environmental Protection Agency
Washington, DC 20460

Paul White
Office of Research and Development
Environmental Protection Agency
Washington, DC 20460

Patricia Van Leeuwen
Toxicologist, Region V
Environmental Protection Agency
Chicago, IL 60604

INTRODUCTION: ORGANIZATION OF THE REPORT

These comments are divided into two main parts, Part 1: General Issues, and Part 2: Detailed Comments. Our comments address many substantial areas of inadequacy in the Madison County Lead Exposure Study report. At the very least, the report needs much more extensive discussion of the differences between study design and actual implementation, better presentation of results, more appropriate statistical analyses of data, and major revisions of the interpretation of the results. Part 1 provides an overview of our concerns. The most important sections are:

1. Implementation of Study Design
2. Field Sampling and Analysis of Samples
3. Statistical Analyses of Data
4. Presentation of Results
5. Interpretation and Conclusions
6. External Review Process

Subsections of each Section are numbered for easier reference. Part 2 of these comments consists of specific comments on certain comments in the text or supporting material, numbered sequentially for easier reference.

PART 1: GENERAL ISSUES

1. IMPLEMENTATION OF STUDY DESIGN

1.1. Recruitment of Subjects

We believe that the report should discuss the possible biases due to recruitment which are inherent in this type of study. While several goals may be defined for the recruitment process, we would expect the process to provide a valid representative sample of children who live in the area of Madison County that is expected to be most heavily impacted by environmental lead exposure. There were a substantial number of households not contacted or no-shows. The report notes that many of these had no telephone. It is likely that many of these households consisted of families with lower socio-economic status (denoted SES in our comments). In other studies, children in families with lower socioeconomic status are known to have a higher risk of elevated blood lead. It is likely that many of these no-contact households were located in older parts of the community and may have had higher soil lead or lead paint exposure. There was also a very high rate of refusals, 266 out of 790 households. Some information on the location of these households would be very useful in determining whether there is a differential rate of refusals or non-contact households that may be confounded with lead exposure.

1.2. Omission of Pontoon Beach Subjects

The study design clearly identifies the importance of a control group. We were disappointed to see that the Pontoon Beach residents were not evaluated. In spite of the fact that these residents lived in newer houses or in a trailer park and were more distant from Granite City, they would still have provided a useful control group with only a modest additional effort.

1.3. Resampling of Children with Elevated Blood Lead

While we are sympathetic to the investigators' concerns about children with elevated blood lead (hereafter defined as blood lead concentration of 10 ug/dl or higher) and are supportive of resampling, this sample is almost useless for inferential purposes. The first difficulty is the well-known problem of "regression to the mean" in follow-up studies. What this means is that if there are repeated measurements on the same child, then even if the mean value for the population remains unchanged between the first and second samples, those children who tested above average on the first test will score closer to the average on the second test, and those children who scored below the average on the first test will tend to score closer to the average on the second test. Thus, the second sample is highly biased for inferential purposes because it includes a few of the siblings of those children with elevated blood lead. Even the siblings with blood lead less than 10 ug/dl at the first test are likely to have blood lead concentrations that are higher than average since they are exposed to the same environment as the siblings with elevated blood lead. The report does not provide any information about this group.

A second difficulty is that in many other studies, children who were tested in winter had lower blood lead concentrations than children who were tested at the summertime peak, typically

by about 30 percent. Even allowing for the hypothetical possibility that there may be a late-winter peak (this hypothesis has not been tested generally), that winter peak must be substantially lower than the summer peak.

Therefore, an observed decrease in blood lead concentrations following intensive education and counselling with the parents or caretakers of the children cannot be demonstrated by this resampling scheme. We do not disagree with the report's hypothesis that parental counselling and education may be effective in reducing blood lead in children exposed to environmental sources of lead. However, this study was not designed to test that hypothesis and cannot be used to do so, nor to estimate the effects of such intervention. A study designed for that purpose would include another group of children with low blood lead concentrations. The study would then randomly assign families to the 'treatment group' (parental education and counselling about environmental lead hazard reduction), a 'positive control group' (parental education and counselling about other child care issues, not emphasizing lead exposure), and a 'negative control group' (no parental education or counselling). A design of this type would control for seasonal changes and age-related changes in blood lead. It should also be noted that intervention has been going on in the area for some time, and the children who took part in this study may have been subject to extensive education prior to the first sampling of blood lead as well.

Since the resampled children in the Madison County study are used to reach some very broad and general conclusions, a much more complete description of the data should have been provided, such as bivariate graphs plotting the blood lead concentrations in September and December. Better yet, with only 61 such children, a table of data values could have been provided.

2. FIELD SAMPLING AND ANALYSIS OF SAMPLES

2.1. Household Dust Samples

The study protocol required collection of 3 to 5 grams of dust using what appears to be an ordinary "dust-buster" type of vacuum cleaner. The priority sequence of collection is well defined (main entrances, two child play areas, and then additional samples from secondary entrances, window sills, furniture, and carpets). However, this differs in many ways from the household dust collection protocols used in other studies. The total dust requirement is much larger than in many studies such as the Urban Soil Lead Abatement Demonstration Project (denoted USLADP) studies in Baltimore, Boston, and Cincinnati. The collection of such a large quantity of dust using a vacuum cleaner of unknown (but presumably low) efficiency will almost certainly require collection of dust samples from the lower-priority areas. We have questions as to how to relate these samples to the child's exposure, which is most likely to occur in the primary play areas (typically, the child's bedroom, the living room or other area used for watching television, and the kitchen). We would have preferred to see the collection of individual samples rather than composite samples of floor dust and window sill dust, since window sill dust often has a much higher concentration and lead loading than floor dust. Our concerns are that this procedure may systematically bias the dust lead measurements, or at worst will greatly increase the variability of such measurements. The report points out this concern as well. Our preference would be to collect separate dust samples from entrances, window sills, window wells, and floors (these may be composited within each type of surface).

2.2. Quality Control for Dust Lead and Soil Lead Analyses

While adequate internal QA/QC procedures for dust lead and soil lead have been defined, it would be useful to have independent external analyses for some of the archived samples. Our experiences in the USLADP studies is that even very good laboratories may not be able to exactly reproduce the concentrations measured at other labs, and that some kind of calibration with respect to consensus values may be needed. It would have been desirable to have done this during the course of the analyses for the Madison County study so as to facilitate comparison with other studies. A reanalysis of a portion of the samples may produce useful information.

2.3. Soil Sample Preparation

The soil samples were apparently not sieved. This makes it more difficult to interpret the results, since small soil particles that can adhere to the child's hands often have higher lead concentrations than larger particles. The removal of paint chips from the soil samples may also have removed a substantial amount of information about sources of lead in surface soil, especially if all samples were not treated equally.

2.4. House Condition and Paint Condition

No examples are presented of what "good" or "poor" condition means. Reproducing this subjective assessment might be impossible. Was yard condition also evaluated? These questions warrant some discussion in the report.

3. STATISTICAL ANALYSIS OF DATA

3.1. There is a Lack of Information about Dependence on Age

The authors note that the incidence of elevated blood lead concentration is at a maximum between ages 1.5 and 2.5 years. However, it appears that when blood lead models are adjusted for age as shown in their Table 10, the adjustment is linear (monotone) and therefore cannot reproduce a peak age. Most studies find large differences at different ages. At least some of the analyses should look at age effects that may be non-linear, either as continuous covariates or in categories (for example, by year or by intervals such as age $<$ 12 months, 12 to 35 months, $>$ 36 months etc.).

3.2. There is Inadequate Spatial Resolution of Demographics and Lead Exposure

The report is almost completely lacking any information about spatial relationships, apart from distance from the smelter. The division of the study area into concentric rings is not defensible. Even assuming that the smelter is a significant point source of environmental lead, it is almost certain that the lead from the smelter was not deposited in a circular pattern around the smelter. Lead particles from the smelter may be transported to a child's residence in many ways: from airborne transport; from rain water runoff; on cars or trains that collected lead dust while near the smelter; in bulk soil transported for use as fill material near the residence; on clothing, shoes, hair, skin, and nails of lead workers or other adults; on outdoor pets. The wind does not blow equally often from all directions; water does not flow uphill; railroad tracks and major highways are not distributed uniformly in the community. There is thus no reason to believe that soil and dust lead will occur in concentric concentration isopleths around the smelter. It is also known that battery casings were used as fill material in various parts of the community, especially the Venice area. This is expected to produce a dispersed random (but non-uniform) additional component of soil lead in Madison County.

An even more important reason for considering other spatial groupings is that the population of potentially exposed children is probably not uniformly distributed around the smelter. The older parts of Granite City are probably closest to the smelter. Thus, housing age, housing condition, and environmental lead from smelter emissions are confounded. Older housing may contain a higher proportion of low-income families and a higher proportion of families with multiple children less than 7 years of age, thus exposing more children to lead than housing units farther from the smelter.

Another factor that may be associated with location is ethnicity, which some studies have found to be associated with elevated blood lead concentration. The clusters of housing where children with blood lead above 10 ug/dl live is clear in the map in Figure 1 of the report, but the reader can only speculate on what these clusters signify. The information was not used in the statistical analyses, apart from distance to the Taracorp facility.

It would be far more helpful to have geographic information about soil and dust lead levels on a smaller scale, say in about 10 contiguous neighborhoods with about 50 children each, including a clear identification of outlying communities such as Madison, Venice, and including Pontoon Beach. One clustering method that would be useful is to identify neighborhoods by contours or concentration isopleths for soil lead. While the authors expressed some hope that the concentric rings of about 1 km radius would do this, we are not convinced that this approach

succeeded. The irregularity in the distances for rings 1 to 3 (0.8 to 1 km) suggest that some neighborhood grouping may have been done, but this is not shown on the map in Figure 1 of the report.

It is well known that important exposure and uptake characteristics of soil lead particles, such as the relative contribution of soil lead to household dust lead and the bioavailability of the soil particles, may depend on properties such as particle size, chemical speciation, and mineral matrix. If there is any possibility that these properties, which affect the relationship between blood lead and soil lead, differ from place to place within the study area due to differences in the primary source of soil lead, then some appropriate basis separating the study area into sub-areas with similar characteristics of exposure and uptake must be found. USEPA uses as a consistent community criterion that less than 5% of the children under the age of six may have blood lead levels equal or greater than 10 ug/dl. In this study community, the entire community blood lead level is high (the percentage of children with a blood lead level of 10 ug/dl or above is 16 percent, or 78/490), and in some areas near and downwind of the smelter it may be even higher, as shown by the map (Figure 1) on the page marked '80' which is actually page 74 of the report. In order to test the feasibility of our recommendation, we did the following simple exercise. We divided the area shown in Figure 1 into 5 spatially contiguous "neighborhoods", as shown on Comments Figure 1, attached. Area 1 extends northeast from the NL Industries/Taracorp facility (NL site) 7 blocks; prevailing winds and proximity to the site make this area a plausible location for deposition of particles. Area 1 is shown by diagonal lines from upper left to lower right in Comments Figure 2. Area 2 is further north and east than Area 1, and is shown by diagonal lines from lower left to upper right in Comments Figure 1. Area 3 is northeast of Area 1 and is at least 3 blocks northeast of the NL site. Area 4 extends south of the site up to about 12 blocks or 1 mile and includes mostly the Madison community. Area 5 is further south and includes mostly the Venice Community. Area 3 is shown by vertical lines on Comments Figure 1, and Area 4 by horizontal lines.

We then expanded the map 200% using a photocopier, as shown in Comments Figures 2, 3, and 4. Even so, it was almost impossible to accurately determine all of the housing units where pre-school children with elevated blood lead resided, shown as open square symbols, and the housing units with no such children shown by solid circle symbols. We counted the number of housing units in each area, as shown in Comments Table 1. The results are that 26 percent of the units in Area 1 have children with elevated blood lead (10/39 units). Only 7 perecent of the children in Area 2, in the same direction but more distant from the NL Industries site than Area 1, have elevated blood lead (9/127 units). Area 3, which is about as close to the site as Area 1 but in a direction which is predominantly upwind, has 12 percent of the units with children who have elevated blood lead. Areas 4 and 5 have comparable incidences, 13 percent of the units in Area 4 (8/60 units) and 14 percent of the units in Area 5 (3/21 units), even though Area 4 housing is about as close as Area 1 housing. The percentage of housing units in Area 1 downwind of the site with lead-burdened children, 26 percent, is significantly higher than the percentage of units about the same distance south of the site in Area 3, 12 percent. This demonstrates that distance alone does not describe the distribution of elevated blood lead in the study area.

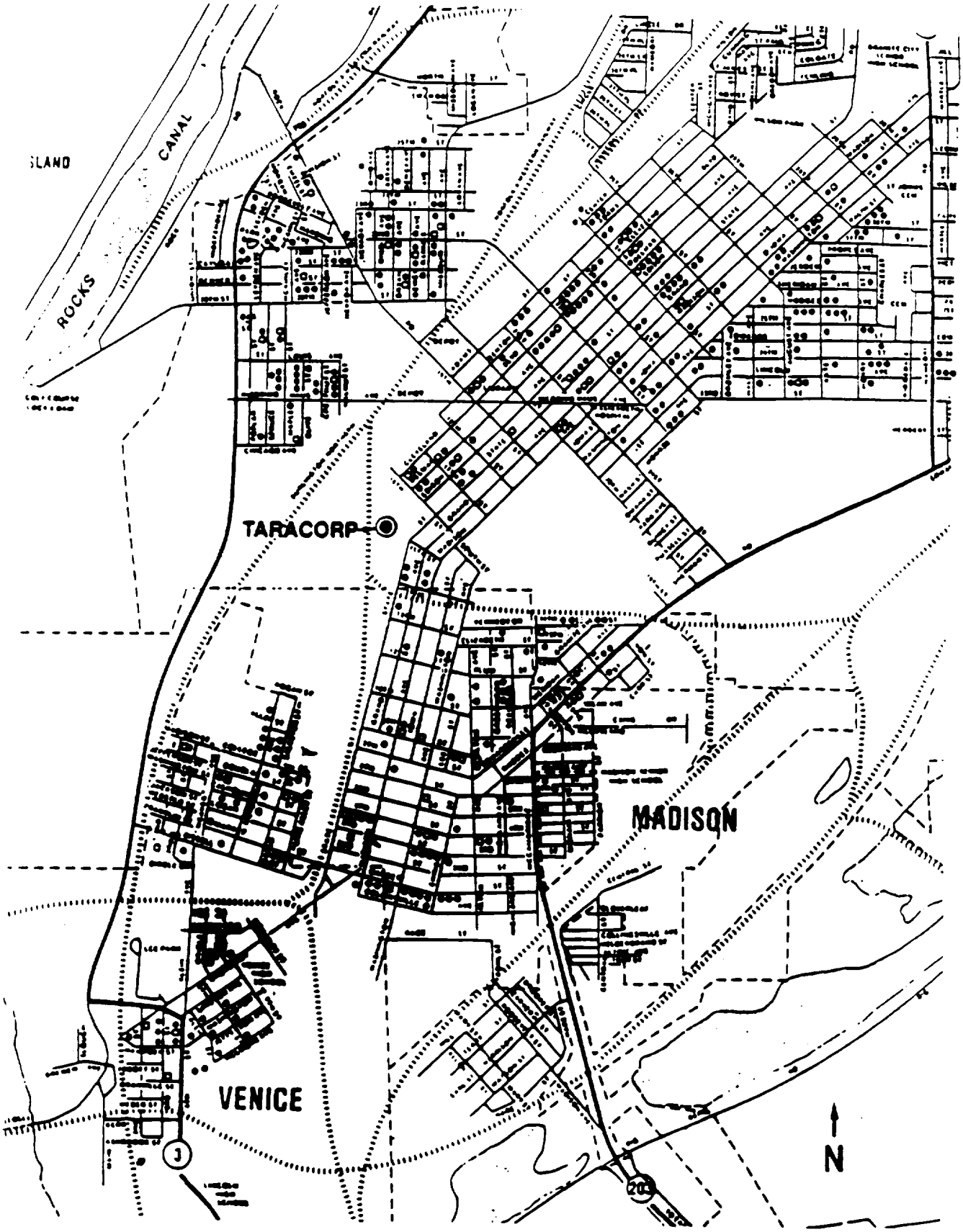
There is no reason why the reader of this report should have to work so hard to extract this absolutely vital information.

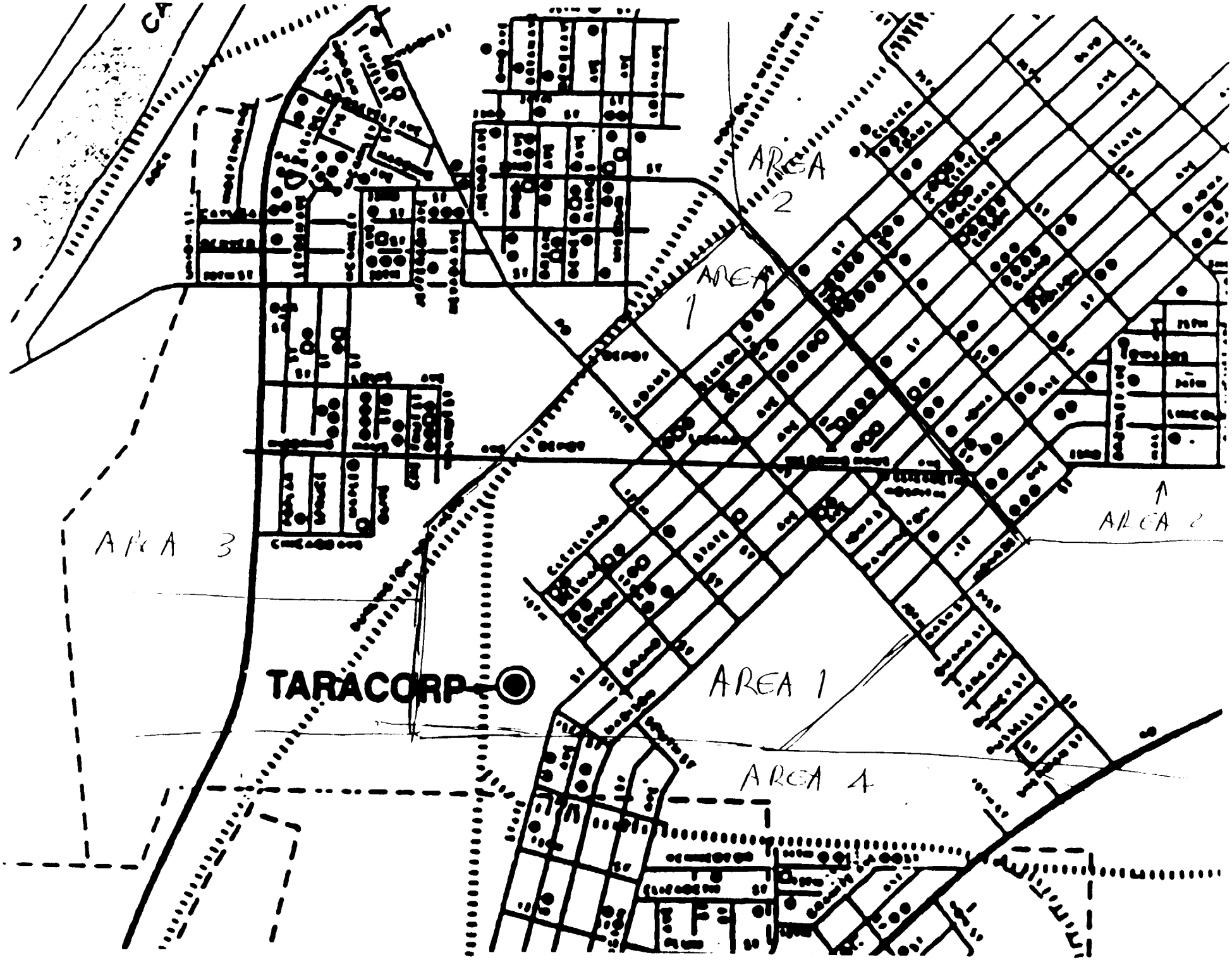
COMMENTS TABLE 1

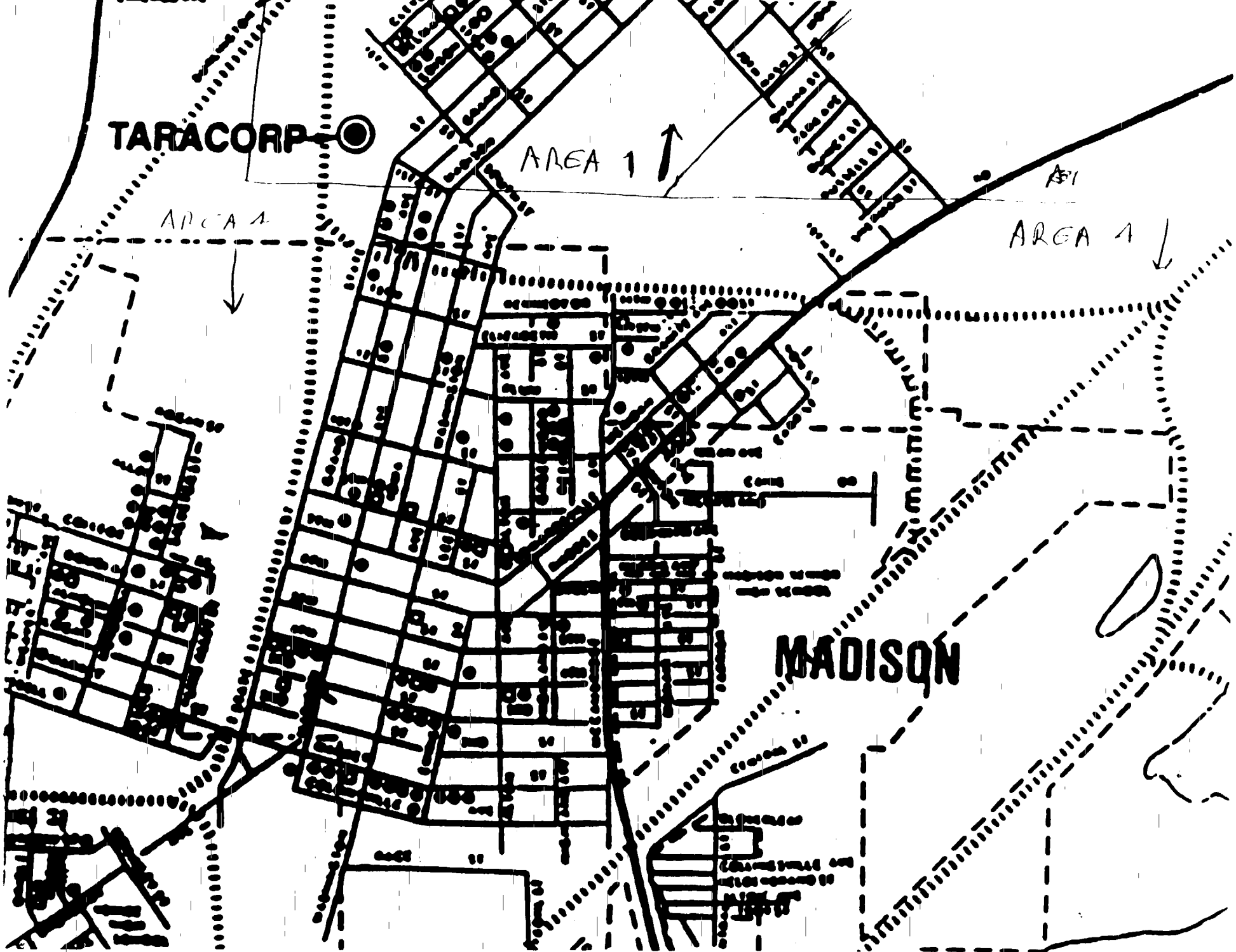
Percent of participating housing units that have at least one pre-school child whose blood lead concentration is greater than or equal to 10 ug/dl. Based on visual counting from map in the Madison County Lead Exposure Study.

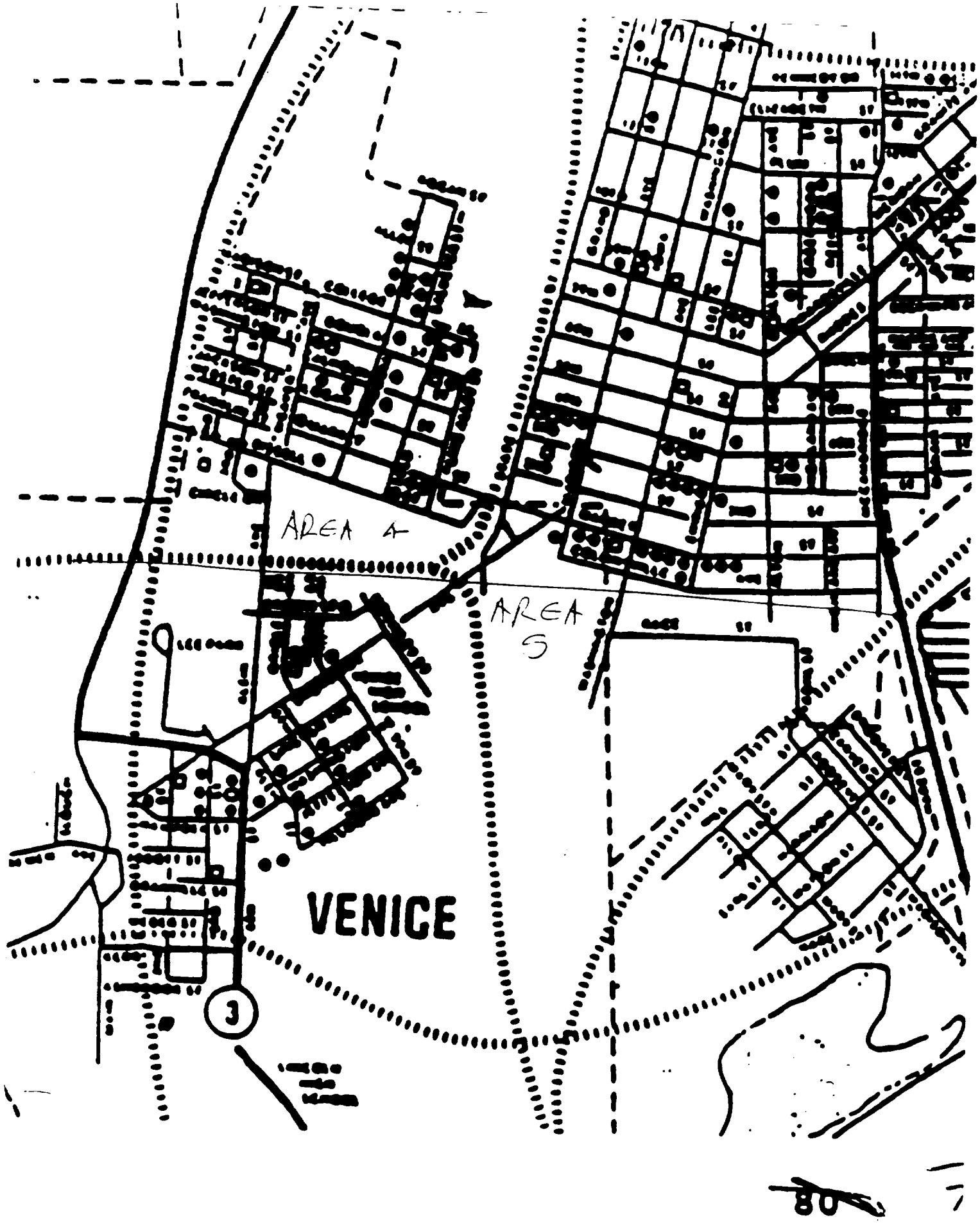
AREA	UNITS WITH CHILD BLOOD LEAD $\geq$ 10 ug/dL	UNITS WITH NO CHILD BLOOD LEAD $\geq$ 10 ug/dL	TOTAL UNITS	PERCENT OF UNITS WITH CHILD BLOOD LEAD $\geq$ 10
1	10	29	39	26 %
2	9	118	127	7 %
3	9	64	73	12 %
4	8	52	60	13 %
5	3	18	21	14 %
ALL MAP	39	281	320	12 %

residents. The closed circles represent residents with children with blood lead levels <0.48 µmol/L (<10 µg/dl). The open squares represent houses with children with blood lead levels of ≥0.48 µmol/L (≥10 µg/dl).




AREA 2
AREA 1
AREA 3
AREA 2
TARACORP
AREA 1
AREA 4


TARACORP
AREA 1
AREA 1
AREA 1
MADISON


AREA A
AREA S
VENICE
3
80

3.3. The Regression Model in the Report Implies Unrealistic Relationships between Blood Lead and Environmental Lead

Lead exposure from multiple media is essentially additive. Therefore, the relationship between blood lead and environmental lead can be well approximated by a linear relationship over a wide range of concentrations, as shown on p. VI-31 in (ATSDR 1988). The statistical reasons for a logarithmic transformation of this relationship are discussed in detail in (Angle et al. 1984) and in (USEPA 1986a) as cited in (ATSDR 1988); the Angle et al. study is also cited in the paper (Weitzman et al. 1993) referenced by the authors. The correct method of fitting the relationship is shown in detail.

The statistical model used by these authors is a serious mis-specification of the correct relationship and may be largely responsible for some of the estimation and hypothesis testing problems that they encountered. Their model may also generate extremely misleading predictions or projections. To illustrate this point, let us use their hierarchical regression model whose coefficients are given by Model 2 on page 70, Table 10, of the Granite City Lead Exposure Study. We may express the model by the equation:

$$\log(\text{blood lead}) = 0.58 + 0.03 \log(\text{water lead}) + 0.03 \log(\text{CXI}) - 0.01 \log(\text{CXO}) +$$

$$0.3\ (\text{Condition code}) - 0.16\ (\text{Refinish Code}) + 0.17 \log(\text{soil lead}).$$

When this model is converted back to the blood lead scale by calculating the exponential function of both the right-hand and left-hand sides of this equation, we have a multiplicative equation, using * to denote multiplication:

$$\text{blood lead} = 1.786 * (\text{water lead})^{0.03} * (\text{CXI})^{0.03} * (\text{CXO})^{-0.01} * (\text{Condition code})^{0.3} *$$

$$(\text{Refinish code})^{-0.16} * (\text{soil lead})^{0.17}.$$

We see that if water lead concentration could be reduced as low as one wanted, nearly down to 0 ppb, then the blood lead predicted by the authors' equation would go down to 0 without controlling the lead in interior lead-based paint (CXI), in exterior lead-based paint (CXO), or lead in soil. This is, of course, absurd. A similar reductio ad absurdem would apply to the other models for log(blood lead) developed by the authors. A model should have been developed so as to avoid these paradoxes.

3.4. The Contribution of Soil Lead to Blood Lead and to Dust Lead is not Correctly Calculated

The hierarchical regression model proposed in the report and described in Table 11 provides an extremely misleading representation of the relationship of soil lead to blood lead. Combination of the models in Tables 10 and 12 of the report provides a much more accurate description of the inter-relationships between blood lead and environmental lead. These analyses show that the indirect relationship between soil lead and blood lead, primarily through dust lead but confounded with other variables in the analyses, may be the most important component of

the blood lead model.

Even if the regression model used in the report were correct (which we have shown to be false), the method used to attribute blood lead to various source terms is not correct. In the first place, the real-world significance of a regression term depends both on its magnitude or effect size, and on its statistical significance. The use of R^2, or the percentage of variance explained by a regression model, describes neither of these. No environmental lead model can be expected to explain an extremely high percentage of the variation in blood lead because this variation is caused by inter-individual differences in lead ingestion, lead absorption, and lead distribution or biokinetics. For a given set of exposure conditions such as environmental lead concentrations in various media, some children who ingest a large amount of lead will have high blood concentrations, and children who ingest a small amount of lead in the same environment will have much smaller blood lead concentrations. As discussed below in Section 3.6, these inter-individual differences are multipliers of environmental lead concentration, and so will contribute about the same of variance to the logarithm of blood lead, whatever the environmental lead concentration. In fact, the 37 percent of variance in the logarithm of blood lead that is accounted for by the regression model in Table 10 of the report (p. 70) is quite comparable to that found in most other studies of the logarithm of blood lead vs. environmental lead.

The single most important predictor of log(blood lead) in Table 10 is the logarithm of the dust lead loading, accounting for 17 percent of the variance by itself. However, the attribution of blood lead increments to other factors are also partial indicators of soil lead or dust lead exposure, such as the variables 'Recent Remodeling' (which suggests recent historical exposure to fine dust particles or possibly surface soil debris), 'Distance' (which shows decreasing blood lead with increasing distance from the smelter and may be a surrogate for smelter-derived airborne deposits of lead on soil and in house dust). To some extent, SES-related variables such as 'Years of Education' and 'Rent or own home', and other socio-demographic variables such as 'Ethnicity' are confounded with soil lead and dust lead. Thus, 17 percent is the minimum contribution of dust lead and soil lead to log(blood lead).

Likewise, soil lead concentration is the most important predictor of dust lead loading, based on Model 2 in Table 12 on page 72 of the report (presumably the logarithm of the composited soil lead concentration, misspelled as 'Soil composition' in Table 12). In fact, soil lead is such a good predictor of dust lead that including soil lead in the dust lead loading equation reduces the contribution of exterior lead-based paint (denoted CXO in Table 12) from statistically significant ($P = 0.02$ in Model 1) to statistical non-significance ($P = 0.2$ in Model 2). It is clear that CXO is thus a partial surrogate for soil lead, probably because lead from deteriorating exterior lead-based paint has been identified as one of the sources of residential soil lead in almost all studies. Soil lead and CXO are correlated, but exterior lead-based paint is probably only a partial contributor to soil lead; the report did not investigate this important question. Other variables used in Table 12 are probably confounded with location and house age, such as the variables 'Condition of residence' and interior lead paint 'Log of CXI'. It is clear that the actual contribution of soil lead to dust lead is much larger than 6 percent of the variance, but the information presented in the report does not allow an estimate of the contribution. The large amount of residual variation in dust lead loading may be attributable to variability in total dust loading which depends on inter-unit differences in the effectiveness and frequency of house cleaning. Dust lead concentrations often show a higher correlation with soil lead concentration than does dust lead loading.

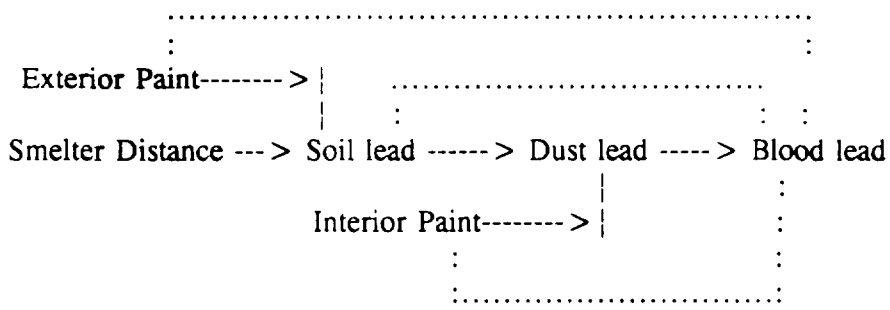
Even if these analyses were correct (see Section 3.3 above), the report has greatly

underestimated the real contribution of soil lead to dust lead, and greatly underestimated the contribution of dust lead to blood lead. Thus, the report has incorrectly used its own analyses. A more complete use of these analyses would demonstrate a very different interpretation - that soil lead is at least a highly significant indirect contributor to blood lead through the dust lead pathway. While the report asserts the importance of this causal pathway in several places, the quantitative significance and magnitude of the indirect pathway from soil to dust to blood is not correctly calculated.

3.5. The Report Does Not Correctly Model Multi-Media and Multi-Pathway Lead Exposure

Lead exposure from soil and paint is a multi-media and multi-pathway process, with household dust as the primary exposure vector for young children. Therefore, any of these sources has both **direct pathways** and **indirect pathways** contributing to childhood lead exposure. Data analyses that fail to recognize that both direct exposure and indirect pathways through dust or soil may both contribute cannot adequately characterize the child's total exposure. This is shown in the ATSDR Report on page II-2 and discussed on pages VI-29 through VI-32 therein. Much more extensive discussion is given in the references cited therein, particularly (Angle et al. 1984) (Bornschein et al. 1985, 1987ab) (Clark et al. 1985, 1987) (USEPA 1986a) (Walter et al. 1980). The Bornschein and Clark papers discuss environmental pathway models, albeit with an incorrect model specification.

The most plausible explanation of the blood lead vs. dust lead and soil lead relationships is that **lead in soil is probably a major reservoir for lead in household dust and so the indirect exposure pathway soil --> dust --> blood should have been used as the basis for blood lead models**. The report notes in several places that "confounding" between household dust lead and lead in soil complicate estimates of the soil effect on blood lead. To a large extent, household dust lead is the most proximate (i.e, the most highly correlated) of the environmental lead concentration or loading variables, based on Table 10 and on the correlations reported in the text on pp. 38-39. Dust is the primary exposure vector. However, dust lead loading is fairly highly correlated with soil lead. Dust lead loading is better correlated with soil lead than with interior lead paint loading in Table 12 on p. 72, but these two variables along with condition of the house allow a fairly good estimate of dust lead loading. It appears then that a pathway model of the following type may be adequate:



The direct pathway from soil lead to blood lead may be less significant in this Granite City study

than the indirect pathway. The strength of the pathways can be estimated and tested for statistical significance using structural equations models or similar techniques. This approach would be far more useful in identifying appropriate goals for environmental intervention.

3.6. The Report Does Not Use Individual Behavioral Variables to Reduce Variance in Blood Lead

While frequently noting the relatively low R^2 values achieved by the statistical models for blood lead, the report overlooked the basis for this fact and its implications for statistical data analysis. The basic problem is that blood lead levels are determined by other factors as well as by environmental lead, such as the child's behavior and biology. This can be stated very clearly *and explicitly, from fundamental biological principles* as described in the EPA Air Quality Criteria for Lead (1986) and elsewhere:

(blood lead increment, ug/dL) = (lead uptake, ug/day) / (blood lead clearance, dL/day)

= (lead intake, ug/d) * (lead absorption fraction) / (blood lead clearance, dL/d)

= (lead concentration, ug/g) * (intake, g/d) * (absorption) / (blood lead clearance, dL/d).

Thus, blood lead increments at any lead concentration in the medium are always proportional to three individually different parameters: the child's media intake or ingestion rate, the child's lead absorption fraction from that medium, and the child's blood lead clearance rate. The fact that lead concentration and other factors account for only a fraction of the variance in blood lead concentration is to be expected. This is irrelevant for risk assessment, however, since the mean blood lead concentration and the number of children with elevated blood lead concentration among a group of children with similar lead exposures can be many-fold different over a range of environmental lead exposures. Lead abatement actions such as the leaded gasoline phasedown of the 1980's and the soil and dust lead abatement in progress in the community of Kellogg, Idaho (which also has an inactive lead smelter) have been very effective in reducing child blood lead concentrations because they reduce the opportunity for exposure among those children who ingest and absorb the largest amount of lead.

This also implies that the regression model could have been improved by including cross-product or interaction terms. Some recent studies (Marcus 1992) suggest that the product of dust lead or soil lead and the relative frequency of mouthing non-food objects may be a better predictor of blood lead than dust lead concentration alone. This information exists in the individual child questionnaire, items 221-230 (pages C-18 and C-19 of the report). This kind of information has been found useful in many other studies, and should have been used in this study to reduce the inter-individual variability and thus better detect the most significant environmental contributions to child lead exposure.

This report needs a much more structured approach to the use of biological and behavioral information. The report notes that older housing, lower income, lower education, greater cigarette smoking, and other behavioral factors are associated with proximity to the smelter site. These factors may also be associated with greater ingestion of soil and dust, and greater oral contact with non-food objects. These socio-demographic factors may also be related

to poor nutrition, thus with increased ingestion (pica for calcium substitutes) and increased absorption of lead. The authors should consider the construction of composite variables such as principal components or factors that can be used to summarize these multi-collinear variables.

Ethnicity is often found to be a significant covariate. This is one of the most significant predictors of blood lead in the Madison County study, as shown in Table 10 of the report. Some effort should be made to identify important confounding variables in this relationship.

3.7. Multi-Collinearity Among Regression Predictor Variables

Many of the predictor variables used in the regression models are highly correlated with each other. This may cause estimates of regression coefficients to be 'unstable', and inflates the estimated standard errors and so reduces the statistical significance of the coefficients. Variance inflation and multicollinearity are discussed in most textbooks on regression methods. The SAS program used for the report has a number of appropriate diagostic statistics for variance inflation and multicollinearity detection that are described in SAS documentation. Many statisticians have eloquently described the problems of model specification using observational data with many correlated predictor variables, particularly econometricians such as Ed Leamer. A paper on modelling strategy that is well known to statisticians who are analysing lead exposure and health effects data was written by Kim Dietrich (1986), "The neurobehavioral effects of prenatal and early postnatal lead exposure", in Steve Schroeder (ed.) Toxic Substances and Mental Retardation. This paper also demonstrates the conceptual advantages of pathway models in a somewhat different context. The authors of this report need to rethink their whole modelling approach.

3.8. The Report Ignores Biases Due to Predictor Measurement

A statististical problem known as "measurement error" or "errors in [predictor] variables" complicates the estimation of regression coefficents. The standard assumption in ordinary least-squares linear regression techniques that were used in this report is that the variables used to predict the response variable (here, log blood lead) are known without error. In fact, environmental lead concentrations generally have a quite substantial measurement error. Part of this is really variability in the chemical analysis, but a larger part of the statistical variability in predictors such as soil lead concentration arises from the difficulty of trying to repeatedly sample at the same place as the original sample, and partly because there are real variations in soil lead at a site at different times. Analytical error could have been studied using the 39 duplicate soil samples. Statistical theory and empirical data shows that the effect of predictor measurement errors on bivariate regression (say, log blood lead vs. log soil lead) is to substantially reduce or attenuate the coefficient from the true value to a smaller value. This is a systematic effect, and produces a biased estimate of the regression coefficient. In multiple linear regression models, when there are measurement errors in several highly correlated predictor variables such as soil lead, dust lead, and house age, then the systematic bias may be either to attenuate or to inflate the regression coefficient, depending on the nature of the inter-correlations among the predictors. Statistical approaches are available (e.g. structural equation modelling methods) that may allow more reliable and less biased estimates of the regression coefficients. Expert statistical

assistance needs to be sought in assessing the likely impacts of measurement error in this study.

4. PRESENTATION OF RESULTS

4.1. Statistical Tables

Many statistical results reported in the text require tabulation. This includes statistics by ring, community, or neighborhood, of all of the variables used in the statistical models. The bivariate correlations reported in the text should also be presented in tabular form, including the statistical significance.

Many comparisons in the text are presented in terms of binary splits such as soil lead above/below 500 ug/g, blood lead above/below 10 ug/dl, and so on. The 2-by-2 tables corresponding to these binary splits would be very helpful in documenting the conclusions in the report.

Regression models should be described more completely, including partial R^2 for each covariate. Serious confounding could be characterized by the largest correlation coefficents among the partial regression coefficients. When variance inflation factors are high, some other regression approaches (such as principal components or ridge regression, easily implemented using SAS procedures) should be used to present an alternative set of relatively different regression coefficients, preferably in an Appendix. This would add a great deal of information with relatively modest efforts. There is not enough detail to assess the validity of any of the regression models. Outlier tests and similar diagnostics should be reported for the benefit of the technical readers. These can be appended as footnotes to tables of regression coefficients.

4.2. Graphs

The graphs in Figures 2a-2b are uninformative and should be replaced. Histograms of blood lead in intervals of 2 or 2.5 ug/dl would be just as easy to interpret and much more informative. Technical readers would probably appreciate a figure with superimposed cumulative distribution functions. Additonal information would be provided by stratifying the sample by age, and by location (community or neighborhood area).

4.3. Maps

Figure 1 is appallingly unclear, considering how much important and useful information it contains. Surely some better-quality method for map production can be found. It would be helpful to present a series of larger-scale maps showing details within each area, such as the location of schools and playgrounds, soil lead isopleths, and so on. Showing the housing units of the participating households, according as they do or do not contain lead-burdened children, would be invaluable to us. Another map showing the locations of non-participating households would be helpful. A number of graphical techniques are available for displaying statistical information on maps, as discussed in Edward Tufte's books. Implementing some of the techniques in SAS/GRAPH or other computer programs is not difficult.

4.4. Confidence Intervals

This report is totally deficient in giving confidence intervals for important effect size estimates or regression coefficients. Significance levels may be useful for hypothesis testing purposes, but these can be indicated by usual conventions such as one-asterisk superscripts for

P-levels between 0.01 and 0.05, and so on. Only readers with some statistical training can readily convert P-levels to confidence intervals.

5. INTERPRETATION AND CONCLUSIONS

pages 53-54, Conclusions: The conclusions do not follow logically from the analyses and findings in the report.

1. We disagree with the conclusion that "Blood lead levels of children under 6 years of age ... were, for the most part, below [10 ug/dl]". With 16 percent of children in the whole study area at or above 10 ug/dl, and a much higher percentage nearer the NL site, some intervention is needed.

2. We agree that "the highest percentage of children with elevated blood lead levels were from 1.5 to 2.5 years of age suggesting that this could be an optimal age for screening". However, this was not used in the regression analyses, since child age was entered as a monotone (non-peaked) predictor of blood lead. It is not clear that the writer of the conclusions was familiar with the results or methods in the text.

3. We agree that "Children with higher blood lead levels lived in houses near the closed smelter ...", but there is not enough information given in the report to reach this conclusion. In fact, the locations in which clusters of cases of elevated blood lead occur are never mentioned in the text. These are located near the site, but particularly in one part of the study area (presumably downwind). The incidence of housing units with excessively lead-burdened children is much higher in this area, compared to a baseline incidence of about 12 percent in other parts of the area mapped in Figure 1 of the study. The reference to the target cleanup area is gratuitous, since it is never shown or discussed relative to the sampling areas defined in the report.

4. We agree that average "soil lead levels decreased as the distance from the smelter increased", but radial distance alone does not describe the pattern of soil lead concentration as a reflection of physical processes of transport and dispersion. This should have been mapped.

5. We agree that "For small children, house dust served as the major vector of exposure. The source of lead in house dust was lead in paint and soil," but the analyses in the report omitted dust lead from the most important statistical models. This omission profoundly distorts and biases the results of the models.

6. It is probably true that "High concentrations of lead in paint in well-maintained houses did not contribute noticeably to lead exposure," but this proposition was not adequately proven in the report. The report confuses many of the analyses by using housing condition as if it were the primary predictor of blood lead and dust lead, whereas housing condition is in reality a modifying factor for the actual lead exposure variables.

7. We agree that "Lead intake was influenced by many personal variables," but this point is irrelevant for risk assessment, as these differences are part of normal inter-individual variability. As discussed in Section 3.6, the analyses in this report failed to use much of the potentially valuable questionnaire data about inter-individual differences.

8. It is probably true that "Education of the parents/guardians ... had a favorable impact on

children's blood lead," but the discussion in Section 1.3 shows that this proposition cannot be proven using data in the study. If true, this may largely explain the reduction in follow-up group. However, several other plausible explanations for the change cannot be precluded since there were no control groups in the study. This question is imbedded in a larger question. There has been a very high level of public awareness of lead hazards for some time because the controversy regarding this site has been going on for a long time. If education and parental counselling is effective in reducing childhood lead exposure, then one might assume that the general awareness of lead hazards through news media presentations and conversation with other people might have had a similar effect, reducing the blood lead concentrations for the community as a whole relative to the same environmental lead concentrations in communities with a lower level of awareness of lead hazards.

9. Relative source contributions cannot be established using the analyses in this report. This is a bottom-line question and requires that the analyses be completely redone. The reported results are highly compatible with the causal model we proposed in Section 3.4, that lead in soil is an important indirect source of lead in blood through the soil-to-dust pathway. Even though the variability in log blood lead is large, so is the effect of different household dust loadings large. These analyses, and in particular other analyses that use correct and appropriate model specifications as outlined in Section 3 of these Comments, are required to correctly estimate total direct and indirect contributions from soil lead and paint lead to blood lead.

6. EXTERNAL REVIEWS

These comments have raised a number of substantive technical issues that need to be addressed. We therefore suggest that reviewers of the next drafts of the Madison County Lead Exposure Study report include individuals with demonstrated technical expertise in these areas, so as provide the authors with appropriate review of their responses to the technical issues we have raised. While we hesitate to name a few individuals among the many qualified scientists, we believe that the following non-government scientists can provide high-quality scientific reviews or can recommend other qualified scientists as reviewers. They include:

Dr. William Gutknecht, Research Triangle Inst. -- methods for dust, soil, paint analysis

Dr. Steven Rust, Battelle Memorial Inst. -- statistical analysis of blood lead studies

Dr. Richard Royall, Johns Hopkins Univ. -- population sampling statistics

Dr. Roderick Little, Univ. Calif. Los Angeles -- design and analysis of sampling studies

Dr. David Jacobs, Nat'l. Center for Lead-Safe Housing -- environmental lead sampling

Dr. Michael Weitzman, Univ. Rochester -- pediatric lead poisoning, design of field studies

Dr. Ann Aschengrau, Boston Univ. -- epidemiology, sample design and analysis

Dr. Mark Farfel, Kennedy Institute, Johns Hopkins -- lead paint sampling

Mr. Ed Norman, Branch Head, Childhood Lead Poisoning Branch, North Carolina Department of Environment, Health, and Natural Resources, Raleigh, NC -- state lead studies

Dr. Joel Schwartz, USEPA, OPPE, on assign to WHO; after 9/1/94, Department of Biostatistics, Harvard School of Public Health -- lead expert on loan to WHO

PART 2. DETAILED COMMENTS

p. 2, para. 1. ABSTRACT: The statement about the lack of effects of soil lead and lead-based paint on blood lead cannot be made as general conclusions. House condition and parental education are confounded with location and house age, thus with distance from the smelter and with lead exposure. The effects of soil and paint lead can be substantially separated from behavioral factors, but not by the analyses in this report. See Part 1, sec. 3.

p. 10, lines 14-15. The use of concentric rings is not justified, since there is no a priori reason to believe that Pb dispersion around a smelter is symmetric. All of our studies around point sources find non-symmetric dispersion as measured by Pb in soil or in dust.

p. 10, last two lines. Not sufficient reason to exclude Pontoon Beach.

p. 11, lines 7-11. Splitting the sample by soil lead concentration isopleths would produce spatially contiguous "neighborhoods", which is a more defensible basis than using soil lead concentration without regard to location. These "neighborhoods" may or may not correspond to separating neighborhoods on the basis of socio-demographic factors that are known to influence blood lead, such as SES, ethnicity, or multi-family vs. single-family housing. Some reasonable spatial separation of these communities into smaller homogenous neighborhoods for statistical analyses should have been attempted.

p. 12, line 1. "The initial definition of sampling regions was somewhat arbitrary ..." Yes! See above. Did this make any difference in sample collection strategy? Show these on Figure 1.

p. 16, line 4. Was the paint condition coded numerically as shown here, 1 = intact, 2 = slightly peeling, ..., 4 = extremely deteriorated? Why not a non-linear coding with higher weight to greater deterioration? Can you provide photographs or drawings to illustrate these levels?

p. 16, lines 7-8. How was house condition coded numerically? See above. Were house condition and paint condition correlated?

p. 16, lines 9-10. The use of a community mean seems a very poor imputation strategy. What about predicting condition from house age, or from block or neighborhood mean? What about the use of dummy variables for missing values? See Rubin & Little's book on missing values. In any case, it is hard to understand why 15% of the values of this easily determined observation are missing, and why the missing values could not be filled in later at minimal cost.

p. 16, lines 15-16. "Obvious paint chips were removed prior to soil analysis." Was this information saved? The causal significance of this finding is that exterior lead-based paint contributes to lead in residential yard soil, which is evident in statistical analyses.

p. 16, last line, p. 17, first 2 lines. "Dust loading" should be used to define the total amount of dust collected per unit area, say as g/sq.m. "Dust lead loading" is the amount of lead per unit area, which is what the report used. The dust lead concentration is sometimes a better

predictor than the dust lead loading, since it often characterizes the presence of a strong dust lead source better than the dust lead loading. From a statistical point of view, dust lead concentration and dust loading constitute distinct "main effects" in a regression or analysis of covariance model, and dust lead loading is their interaction term. These may all be separately predictive of blood lead., albeit correlated.

p. 19, para. 1. Note that the interior paint score is the interior XRF reading times a four-level paint condition index, whereas the exterior paint score is the product of the exterior XRF reading times a three-level house condition index. Some explanation is needed.

p. 19, lines 7-8. Distance from smelter is not an adequate measure of spatial dispersion.

p. 20, lines 9-10. A better strategy would be to dichotomize data by neighborhoods, even if "neighborhoods" are defined by soil lead concentration isopleths. Even the reporting of statistics by community (Granite City vs. Venice vs. Madison) would be useful to the reader.

pp. 20-21. The hierarchical regression strategy developed in this report should be dropped, or should be justified in much greater detail. There are many possible data-driven approaches to variable selection in multiple regression, and different approaches can produce different sets of "optimal" coefficients as is demonstrated in most texts on multiple regression (Draper and Smith, or Daniel and Woods). This is a consequence of the correlation among predictor variables, since there is some fraction of the variance of the logarithm of blood lead that could be explained equally well by any of several predictors. A directed hierarchical regression strategy can only be justified on the basis of a postulated causal model. A plausible model is suggested by the report's exploratory analyses for blood lead (Table 10) and dust lead loading (Table 12, model 2), as sketched in Part 1, Section 3 of these comments. The structural equation modelling approach recommended in Section 3.5 is statistically unbiased and is a much more efficient method for estimating parameters in causal hypothesis testing.

p. 21, lines 4-7. Controlling for correlated covariates is one of the most important modelling issues in analysis of any observational study. The most common approaches, such as stratification or dimensionality reduction, are easily implemented using SAS. The "neighborhood" approach we suggested above should largely control for distance of smelter, age of house, socio-economic status (SES) and other variables, and is more appropriate to the scale of environmental assessments being carried out. Constructing composite variables by principal components analysis or otherwise may also be used to reduce dimensionality of the problem. However, the real problem is that soil lead and dust lead are separate media, but they are correlated. Both contribute to child blood lead by different pathways. The soil lead is a contributing fraction to dust lead. Blood lead is more highly correlated with dust lead than with soil lead. This suggests that soil lead is less important as a direct exposure medium than dust lead, but that soil lead is clearly a significant source for dust lead.

p. 22, lines 4-8. Why couldn't the analyses have been done with and without Pontoon Beach as a control group? See Section 1.

p. 23, para. 1. Does the non-participation group have different characteristics than the others

who participated? This question needs quantitative analysis, not anecdotal reports. What efforts were made to obtain more information about non-participants so as to compare them with participants? This may be a systematic source of bias.

p. 23, line 4. The non-participants' responses to USEPA actions should have been irrelevant. Did the interviewers fail to communicate the purposes of this study? In view of the long (five to six year) community awareness of the proposed EPA actions, the interviews should have been structured so as to clearly define the purposes and missions of the study sponsors. The proposed goals of the study are defined in the consent form (Page B-8). While the sponsors of the study are listed, this introduction does not seem to provide a characterization of the purpose of this study as distinguishable from the proposed cleanup actions. We are concerned that this may have contributed to the high non-participation rate.

p. 23, para. 2. There are certainly some suggestions that the non-response was correlated with biasing factors. For example, lines 10-11, one may presume that the families without telephones had lower SES or lower income, thus their children are more likely to have higher blood lead. The non-response sampling bias issues are known to every epidemiologist. Please discuss.

p. 24, para. 1. Reporting the numbers in the text makes it very difficult for most readers to determine the composition of the participating households. It would be useful to tabulate this in a two-way table, with the row factor giving the number of participating children less than 6 years in the household (0, 1, 2, or 3+) and the column factor giving the number of participating youths in the household (0, 1, or 2+). The number of families with pre-school children 230 (1 child) + 106 (2 children) + 14 (3 or more) = 350 familes/households, thus we have 388 - 350 = 38 households with no participating pre-school children. Please reconcile all numbers.

p. 24, lines 6-8. Location is important. Where were the multiple-sibling households located?

p. 24, lines 13-14. Location is important. Where were the ethnic (primarily African-American) families located?

pages 24-26, Participant Characteristics. Please provide tables for all of these cross-tabulations. Were any of the analyses stratified by subpopulation?

pages 25-26. Need to understand collocation of participant characteristics, many seem to be common measures of SES.

page 27, para. 1. The aggregate mean blood lead concentrations and percentages of children with elevated blood lead are almost meaningless without breaking out the location of the children. For example, if the Pontoon Beach children had been included in the study, would their presumably lower blood lead concentrations have been averaged in with all of the other children, thereby lowering the blood lead average even further? The important question that these statistics overlook is the spatial dimension of the elevated blood lead cluster, which is evident from the map in Figure 1 of the report. The map is almost impossible to read, but we counted (about) 39 houses or residential units in which children with elevated blood lead (at least 10 ug/dl) lived, out of a total of (about) 320 units, or 12 percent of the units. See Part 1,

Section 3.1 above. The averages should also have been adjusted for the differential non-participation rates in the different areas.

page 27, lines 12-15. Compare blood lead concentrations of ethnic groups after adjustment for neighborhood or SES or environmental lead.

page 28, para. 2. The repeat blood sample study needs to be adjusted for several reasons: (1) winter blood lead is almost always about 30 percent less than summer peaks; (2) "regression to the mean" because of sampling variability; this could have been evaluated if a similar sample of children with low blood lead had been taken; (3) the September study was itself a significant intervention activity that increased the parents' or caretaker's awareness of lead hazards. These are discussed in detail in Part 1, section 1.3.

p. 31, 4 lines from bottom. Many missing data on house age. How imputed? Were missing cases dropped from the analyses?

p. 32, lines 7-13. This is a completely inappropriate way of presenting the data. It would have been much more informative to have presented the percentage of children in each area with blood lead concentrations of 10 ug/dl or greater.

p. 32, lines 14-15. This is an extremely misleading statement. We agree that housing condition is a covariate that may affect lead exposure. However, without lead in some medium such as soil, dust, or paint, housing condition is at best a weak indicator of differential exposure to other lead sources because it is confounded with SES and other factor. If there is no lead in the house, there is no exposure to household lead. Housing condition should be treated statistically as an interaction term or confounder.

p. 33, para. 1. The report indicates the range of soil lead concentrations for composited samples. The range of soil concentrations from multiple samples within a yard is likely much larger. These 'hot spots' may indicate potential exposure sources beyond those suggested by the composite sample concentration.

p. 33, line 10. Is the difference of 89 ppm within specifications?

p. 33, line 15. Were the log-transformed data actually tested for normality? We are concerned that, because there may be different mixtures of lead sources in different parts of the Madison County sampling area, even the log-transformed data may not be log-normally distributed. What implications does the possible deviation from log-normality have for the statistical analyses?

pp. 36-39. Present results of binary splits in Tables. Present tables of correlation coefficients. Specifically identify missing value imputation or deletion strategies.

pp. 36-39. The binary splits that are most informative are those that divide children above and below 10 ug/dl. These must be tabulated.

p. 37, para.1. Use of the symbol 'r' for correlation must be explained for most readers.

p. 38, para. 2. Doesn't the strong and similar correlation of log(soil lead) with log(dust lead loading), log(1/distance), and house age (log transformed or not?) suggest a common factor?

p. 38, lines 5-6. The high correlation of soil with indoor lead paint may represent a secondary relationship because of a strong confounding with house age. Why comment on this, and then gloss over the much stronger and physically explicable correlations with distance and house dust lead loading?

p. 39, last para. The use of building condition as a primary predictor of blood lead is a very poor choice. This variable is highly confounded with many other variables, such as housing age and SES, that appear to be highly correlated with environmental lead **in the Madison County study, but not in general**. The report overlooks a basic axiom of exposure assessment: There is no exposure to a chemical if the chemical is not present. Even a badly deteriorated building does not pose a lead hazard if there is no lead in the paint or construction materials, no lead in surrounding soil, no lead in floor or furniture or carpet or window dust, no lead in the water supply. Building condition should be used as a modifier of exposure. The association of building condition, building age and SES may explain other correlations.

p. 40, para. Cigarettes per Day. Correlations with dust lead etc. probably represent confounding with SES and location.

p. 41, Regression Analysis para. Regression analysis is limited in its ability to deal with many correlated factors, as noted elsewhere. Environmental pathway analysis using structural equation system methods deals with this much more effectively, and also allows for adjusting the regression coefficients for the effects of "measurement error" in the predictor variables.

p. 41, Stepwise Regression para. How were the variables on the list selected?

p. 42, last 4 lines. If the stepwise regression method is not going to be used for the only thing that it can do well, why report the results? See Part 1, Section 3.7, and especially the predictor variable selection strategy discussion in the Dietrich et al. paper cited there. The stepwise regression model described in Table 10 is actually far superior to the hierarchical model proposed in the report, and in fact does capture the biological and environmental relationships much more effectively than the model in Table 12. It's still not right; see Part 1, Section 3.4.

p. 43, lines 12-13. "... house dust was not included as a potential confounder since the source of lead in dust was mostly paint and soil." This is a a major conceptual blunder, with serious consequences, and largely invalidates the analyses. See Part 1, Sections 3.4 and 3.5.

p. 43, para. 2. This is an extremely idiosyncratic collection of predictors for a hierarchical model. Exterior lead-based paint is strongly correlated with soil lead, probably representing a source term. Interior lead-based paint is strongly correlated with dust lead, probably causally, and is thus a predictor of blood lead, as is recent household refinishing. Water lead is a weak

predictor, confounded with house age and thus with building condition. We do not understand the justification for inclusion of confounding terms and omission of the most important direct predictor, household dust lead. See Part 1, Section 3.7, on modelling strategies.

p. 43, bottom line and p. 44, top 2 lines. The small R^2 values are attributable to the report's failure to appropriately include household dust as the primary exposure vector. Not surprisingly, since the analysis omitted the most important (but indirect) process in childhood soil lead exposure, it found a fairly small direct effect for soil lead. Much of the soil lead effect is buried in the confounded variables used in Model 1, especially the logarithm of CXI and the House condition. Since the regression model is not correctly specified, the conclusion about the direct effect of soil lead on blood lead may or may not be true; it is certainly irrelevant because soil lead is the most significant cause of dust lead, and dust lead is by far the stronger predictor of blood lead. See Part 1, Section 3.

p. 44, para. The Contribution of Soil Lead to Dust Lead. The authors' mis-specification of a total exposure model invalidates their analyses separating the paint contribution from the soil contribution to house dust. Since exterior lead-based paint is often a substantial source to lead in soil, the inclusion of an exterior lead-based paint term in the analysis proxies out a major part of the soil contribution to household dust. An appropriate multi-media pathway model would allow better separation of these effects. This study threw away an opportunity to obtain some direct information on the contribution of exterior lead-based paint on soil lead by sieving the paint chip particles out of the soil samples. Building condition is probably an important modifying factor in dust lead loading and in dust loading, but without lead from identifiable sources in soil and paint, there would be much less lead in dust whatever the condition of the house. Building conditon is a composite of interior and exterior paint condition, but one or the other of the component indices may be more predictive than the composite index; was this tested? Were the separate effects of paint condition and XRF reading tested? It seems unusual to include the product term ('interaction effect' in a statistical analysis) without including the separate terms ('main effects') as additional factors.

p. 44, para. on multiple children, and Table 13, page 79. Without adjustments or stratification for important confounders such as SES or neighborhood, this comparison is not very meaningful.

p. 45, para. 1. The purpose of the study, as stated here - "to determine whether children, under the age of six years, living in an environment with elevated lead levels in soil had elevated blood lead levels", is not the same as the objectives stated in the protocol submitted in 1991. The Protocol for the Multistate Lead Exposure Study, Illinois, Kansas, and Missouri, which should be part of this report, lists the following objectives:

"1. To determine the dose measures of lead and cadmium in blood and urine in target populations and compare them with dose measures found in comparable populations.

2. To determine the level of lead and cadmium of environmental media in target areas and compare these with levels of contamination observed in comparable non-target areas.

3. To characterize the distribution of selected biomedical test values in target area populations and compare them with the distribution of biomedical test values observed in comparable area populations.

4. To compare the distribution of selected biomedical test values in target and

comparable populations and compare them with standard reference ranges for these tests.

5. To determine the extent to which environmental, behavioral, occupational, and socio-economic factors influence exposure to lead and cadmium in target and non-target populations.

6. To determine the extent to which internal dose measurements of lead and cadmium in blood and urine are associated with the distribution of biomedical test values.

7. To determine the extent to which exposure has occurred in populations living in areas with both mining and industrial emissions compared to populations living in areas with industrial emissions only."

It is questionable whether conclusions on questions which the study was not designed to answer are valid. However, given the stated purpose of the report, it should have at least answered the question, whether the study observed a difference in the percentage of yards with soil lead levels greater than/less than 500 ppm for children whose blood lead levels are greater than 10 ug/dl as compared to yards with soil lead levels greater than/less than 500 ppm in children whose blood lead levels are less than 500 ppm.

p. 45, para. 2. The demographic differences between most-exposed and least-exposed children should be emphasized.

p. 45, second sentence from bottom. Cite references for reduced lead in gasoline.

p. 45, 2 lines from bottom. "lead exposure factors do not occur in isolation." A key point, not adequately handled in the analyses.

p. 46, last sentence. The comment about mean blood lead of 5 ug/dl is irrelevant to health risk assessment. The finding of 6.9 ug/dl in the Madison County study is more relevant, but still misses the point. The real point of the study is that 26 percent of the houses in our Area A defined in Part 1, Section 3.2, have children whose blood lead concentrations exceed 10 ug/dl, which is a **health-based blood lead level of concern.** Furthermore, these children are found in an area in which soil lead concentrations and other lead exposure indices are relatively high.

p. 47, lines 1-11. Irrelevant. The current blood lead level of concern for EPA and CDC is 10 ug/dl, and that should be used as the reference value for all health risk assessments in the report. The older blood lead levels of 25 ug/dl are now known to be unsafe and do not merit any further discussion. In the 1960's, 40 ug/dl was considered safe, whereas the current CDC guidelines mandate medical treatment at 45 ug/dl and above. Stay with 10 ug/dl as a health effects level.

p. 47, last two sentences in para. 1. The errors in analyses described above invalidate these "findings". Behavioral factors are important **modifiers** of exposure. But, if there were no lead in the environment, there would be no exposure, and that is not the case in Granite City since many children had elevated blood lead: 16 percent in the whole area; 19 percent among African-American children; and probably a much higher percentage closer to the smelter, since 26 percent of the housing units had children with elevated blood lead concentrations.

p. 47, second para. Education of parents is a significant component in awareness and avoidance of lead hazards, and may be a better modifier of exposure than income or other partial indicators of SES (socio-economic status, possibly as measured by the Hollingshead index).

p. 48, line 11. "House dust was ... not included in the hierarchical regression against blood lead." This therefore invalidates any other findings from that model.

p. 48, lines 14-16. "Simultaneous regression ... would have produced unpredictable [unstable] and invalid partial regression coefficients." The mis-specified form of the model used in the analyses may have created the problem. A pathway model with additive effects from paint, soil, and dust, and multiplicative modifiers from house or paint condition and behavioral variables, would probably have reduced the problem of multi-collinearity and provided a better basis for judging whether the lead sources near the smelter are similar in effect to those farther away. See Part 1, Section 3.

p. 48, last para. The variables that were discarded in the analyses (age of child, hours spent outdoors, and child behavior) are precisely those that are most useful in reducing the inter-individual component of variability in blood lead. See Part 1, Section 3.6.

p. 49, line 5. "37 % of the exposure ..." The authors should have said "37 % of the variance in the logarithm of blood lead"

p. 49, lines 6-8. By ignoring the soil-dust-blood pathway, the report greatly underestimates the role of soil as an indirect source of lead in blood. We have described above how the inclusion of house condition as a confounding variable is very inappropriate. The conclusion that the maximum contribution of soil is 3 percent is unwarranted; this is a minimum contribution, and a substantial underestimate. By the same fallacious arguments presented in the report, the maximum contribution of lead-based paint is also 3 percent at most. Actually, neither conclusion is correct since the analyses on which the conclusions are based are so badly flawed. This paragraph needs to be completely revised.

p. 50, lines 3-12. This section needs to be rewritten. A candid description of the failures of the authors' modelling strategy would explain the instability of the regression coefficients. See Part 1, Section 3.7.

p. 50, last 2 lines, and p. 51, lines 1-8. As explained in Part 1, Section 1.3, the follow-up data cannot be used to test the hypothesis that intervention was responsible for the decrease in blood lead concentration. Other explanations, such as regression to the mean and the impact of initial recruitment in the study cannot be precluded as explanations. This study was not designed to test the effectiveness of intervention, and lacks the control groups that would allow valid inference about intervention.

p. 51, lines 4-8. If the summer blood lead peak in Madison County had passed, then peak blood lead concentrations should be even higher than observed in this study. We would expect about a 30 percent decrease to winter low values, even if a hypothetical winter peak exists.

p. 51, para. 2. Many behavioral factors affect the seasonal variations in blood lead, which we still see in the control groups in the USLADP cities. Seasonal variation of blood lead in these recent longitudinal studies are still at about 30 percent of the annual average concentration. Blood lead concentrations in most longitudinal studies increase up to ages 18 to 36 months, then

decrease (the regression models used in this report did not adjust for a non-linear relationship with age). Large reductions in blood lead associated with environmental abatement have occurred in some recent studies, such as Kellogg ID, and greatly exceed any possible blood lead measurement error. The 15 percent decrease in blood lead associated with soil and dust abatement in the Boston USLADP study greatly exceeds the measurement uncertainty associated with the mean of a sample of 150 children. The seasonal variations and abatement effects are real and should be discussed in the report.

p. 51, para. 1. The discussion on seasonal fluctuations is incomplete. The discussion on the changes in blood lead from abatement or removal (of child or of source) is extremely distorted and does not reflect the large reductions in child blood lead in other smelter communities, such as East Helena MT and in Kellogg ID, following either remediation or parental awareness intervention or both.

p. 52, para. 1. The magnitude of the fluctuations in repeat sampling and the magnitude of the analytical errors, including drift, should be included in the discussion if this is relevant to the Study report. The relevance of this paragraph is unclear. If not needed, drop it.

pp. 53-54. Conclusions do not follow from the analyses. These are discussed in Part 1, Section 5.

p. 70, Table 10. log blood lead level? Also, use 'log of dust lead load'.

p. 71-73 "Soil composition" is clearly a misnomer. The correct entry is 'logarithm of soil lead concentration in composite sample'.

p. 74. Mislabelled as p. 80. See Part 1, Section 4.

pp. 75-76. These are terribly misleading plots. Use ordinary histograms of blood lead by age.